

SORTING PARTICLES IN PARALLEL

BACKGROUND

[0001] Cells and other particles are often obtained as mixtures of two or more different types. For example, blood or tissue samples from patients may include a mixture of many different cell types that mask the presence or properties of a particular type of cell that is of interest. Accordingly, the cells of such samples may need to be sorted with a cell sorting device, such as a fluorescence-activated cell sorter, to identify, purify, and/or characterize cells of interest in the samples. However, cell sorters can be expensive and complex to operate and maintain.

BRIEF DESCRIPTION OF THE DRAWINGS

[0002] FIG. 1 is a schematic view of a system for sorting particles, in accordance with an embodiment of the invention.

[0003] FIG. 2 is a schematic view of a sorter unit that may be included in the system of FIG. 1, in accordance with an embodiment of the invention.

[0004] FIG. 3 is a schematic view of another system for sorting particles and particularly cells, in accordance with an embodiment of the invention.

[0005] FIG. 4 is a partially schematic view of the system of FIG. 3, in accordance with an embodiment of the invention.

[0006] FIG. 5 is a bottom view of selected portions of a substrate assembly included in the system of FIG. 4, in accordance with an embodiment of the invention.

[0007] FIG. 6 is a fragmentary bottom view of a sorter unit included in the substrate assembly of FIG. 5, as the sorter unit sorts cells, in accordance with an embodiment of the invention.

[0008] FIG. 7 is a fragmentary sectional view of the sorter unit of FIG. 6, taken generally along line 7-7 of FIG. 6, in accordance with an embodiment of the invention.

[0009] FIG. 8 is a bottom view of a manifold disposed above the substrate assembly of FIG. 5 in the system of FIG. 4, in accordance with an embodiment of the invention.

[0010] FIG. 9 is a bottom view of an upper layer of the manifold of FIG. 8, in accordance with an embodiment of the invention.

[0011] FIG. 10 is a sectional view of the manifold of FIG. 8, in accordance with an embodiment of the invention.

DETAILED DESCRIPTION

[0012] A system, including method and apparatus, is provided for sorting particles, such as cells, in parallel. The system may include a device having a plurality of sorter units that operate in parallel. The sorter units may receive particles from parallel conduits in fluid communication with the same input reservoir. Each sorter unit may be configured to sort particular particles to a different pathway (or pathways). Particles and/or fluid may be transported from the input reservoir by a transport mechanism that moves particles and/or fluid in parallel through the parallel conduits. The transport mechanism may operate, for example, by

exerting pressure on fluid and/or by exerting a force selectively on the particles relative to the fluid. The use of sorters that operate in parallel may substantially increase throughput of particle sorting.

[0013] FIG. 1 shows a system 20 for sorting particles using a plurality of “n” sorters 22 configured to operate in parallel. The system may include any suitable number of sorters including only one. The sorters may be disposed in parallel fluid communication with an input reservoir 24 holding an input mixture 26 of two or more types of particles, such as particles A and B, in a fluid. Fluid communication between the input reservoir and the sorters may be provided by a conduit network 28. Portions of the input mixture may be directed to the various sorters from the conduit network as separate streams of particles. Each sorter may selectively move the A and B particles of a stream along different paths 30, 32, so that the mixture is enriched for A or B particles, respectively, in different intermediate sites 34. Sorted particles of each type from each sorter may be combined, shown at 36, so that A particles and B particles are directed to their respective receiver structures 38, 40.

[0014] A sorter may be any device or mechanism for enriching a particle mixture for at least one type of particle in the particle mixture relative to other types of particles in the mixture. The sorter may be configured to move one or more types of particle from a default path of particle/fluid movement to an alternate path (or a plurality of alternate paths). Alternatively, the sorter may move different types of particles from a default path of movement to different alternate paths according to the type of particle.

[0015] The sorter may apply a force on a fluid volume or fluid segment in which a particle is disposed or may apply a force on the particle selectively in relation to the fluid volume. The force may be a pressure exerted on the fluid volume, a dielectrophoretic force on the particle, an electroosmotic force on the fluid, etc. In some embodiments, the sorter may sort by changing the path followed by fluid and particles, for example, for opening and/or closing valves, among others.

[0016] Sorters may be configured to operate concurrently, for parallel sorting from an input mixture. Alternatively, or in addition, sorters may be disposed in series for sequential sorting, for example, to provide progressive enrichment of a mixture for a particular type of particle. Enrichment, as used herein, may include any increase in the representation of one particle type relative to one or more other particle types of a mixture. For example, enrichment may increase the representation of a particular type of particle from a lower to a higher percentage of the particle total, and/or may substantially or completely separate the particular type of particle from one or more other types of particles.

[0017] An input reservoir may be any vessel (or vessels) configured to receive the input mixture and release portions of the input mixture to a sorter(s). Release of the portions may be passive, such as through passage that is always in fluid communication with the input reservoir, or active, such as with valve that operates to release portions selectively. The input reservoir may be a well, a chamber, a channel, a syringe, etc.

[0018] A conduit network may be any set of passages that provide fluid communication between the input reservoir